REMARKS

In view of the above amendments and the following remarks, reconsideration of the outstanding office action is respectfully requested. Pursuant to 37 CFR § 1.121, attached as Appendix A is a Version With Markings to Show Changes Made.

In natural populations, most phenotypic variation is continuous and effected by alleles at multiple loci. Although this quantitative variation fuels evolutionary change and has been exploited in the domestication and genetic improvement of plants and animals, the identification and isolation of the genes underlying this variation has been difficult.

The most conspicuous and, perhaps, most important quantitative traits in plant agriculture are those associated with domestication. Key adaptations to survival in the wild were dramatically modified by early humans; fruit-bearing crop plants are a prime example. Dramatic and relatively rapid changes in fruit size have accompanied the domestication of virtually all fruit-bearing crop species, including tomato, watermelon, apple, banana, grape, berries and a vast assortment of other tropical, subtropical, and temperate species. These changes have benefited mankind but have often been at the expense of the plant's seed production, dispersal, and survival under natural conditions. The progenitor of domesticated tomato (*Lycopersicon esculentum* Mill.) most likely had fruit less than 1 cm in diameter and only a few grams in weight. Such fruit were large enough to contain hundreds of seeds and yet small enough to be dispersed by small rodents or birds. In contrast, modern tomatoes can weigh as much as 1,000 grams and can exceed 150 cm in diameter. While it is known that the transition from small to large fruit occurred numerous times during the domestication of crop plants, and that it is quantitatively controlled, the molecular basis of this transition has thus far been unknown.

Using the approach of quantitative trait locus (QTL) mapping, most of the loci involved in the evolution and domestication of tomato from small berries to large fruit have been genetically mapped. One of these QTLs, *fw*2.2, appears to have been responsible for a key transition during domestication: all wild *Lycopersicon* species examined thus far contain small fruit alleles at this locus whereas modern cultivars have large fruit alleles. What is needed to further the current understanding of the genetic regulation of fruit size in plants is the identification of the nucleic acid sequence of the *fw*2.2 gene and of the protein product

encoded by the cDNA of that gene. The present invention is directed to achieving these objectives.

The election of Group I (i.e., claims 1-2 and 4-49) is confirmed. Applicant has cancelled claims 3 and 50-55 without prejudice to filing them in a divisional application.

The rejection of claims 1-2, 4, 7-8, and 11-49 under 35 U.S.C. § 112 (1st para.) for lack of written description is respectfully traversed in view of the above amendments.

Claim 1 and claim 8 have been amended to incorporate the allowed subject matter of claims 5-6 and claims 9-10, respectively. In addition, claims 1 and 8, as amended, include the limitation of a nucleic acid molecule which hybridizes to the nucleic acid molecule having a nucleotide sequence of SEQ. ID. No. 1 or No. 3, respectively, "under stringent conditions characterized by a hybridization buffer comprising 0.9M sodium citrate buffer at a temperature of 45°C." Applicant submits that this limitation is sufficiently described in the specification. In particular, the conditions for hybridization are taught in the instant application at page 8, lines 4-9. Furthermore, applicant submits that one skilled in the art would fully understand, based on applicant's description of the claimed nucleic acid molecules on pg. 4, line 20 to top of pg 5, pg. 6, lines 6-19, and Examples 4-5 of the present application, what nucleic acid molecule would be capable of hybridizing to the nucleic acid molecule having a nucleotide sequence of either SEQ. ID. No. 1 or No. 3 in accordance with the claims.

For all these reasons, the rejection of claims 1-2, 4, 7-8, and 11-49 under 35 U.S.C. § 112 (1st para.) for lack of written description should be withdrawn.

The rejection of claims 1-2, 4, 7-8, and 11-49 under 35 U.S.C. § 112 (1st para.) for lack of enablement is respectfully traversed.

Page 5-6 of the outstanding office action acknowledges that the specification is enabling for claims drawn to "an isolated *Lycopersicon pennellii* ORFX gene of SEQ ID NO: 1 encoding SEQ ID NO: 2 and an isolated *L. esculentum* ORFX gene of SEQ ID NO: 3 encoding SEQ ID NO: 4 and tomatoes transformed therewith . . .." However, the specification is deemed non-enabling for any other nucleic acid molecules encoding a protein that regulates fruit size, or for the transformation of other plants. In the latter regard, applicant respectfully disagrees.

In particular, the PTO states that the specification fails to provide guidance for other genes that can be used to regulate fruit size and/or cell division. However, as amended, claim 1 is now limited to "[a]n isolated nucleic acid molecule encoding a protein which reduces fruit size and/or cell division in plants, wherein the nucleic acid molecule either: 1) has a nucleotide sequence of SEQ. ID. No. 1; 2) encodes a protein having an amino acid sequence of SEQ. ID. No. 2; or 3) hybridizes to a nucleic acid molecule having a nucleotide sequence of SEQ. ID. No. 1 under stringent conditions characterized by a hybridization buffer comprising 0.9M sodium citrate buffer at a temperature of 45°C", while claim 8 is limited to "an isolated nucleic acid molecule, wherein the nucleic acid molecule encodes a protein which increases fruit size and/or cell division in plants, and the nucleic acid molecule either: 1) has a nucleotide sequence of SEQ. ID. No. 3; 2) encodes a protein having an amino acid sequence of SEQ. ID. No. 4; or 3) hybridizes to a nucleic acid molecule having a nucleotide sequence of SEQ. ID. No. 3 under stringent conditions characterized by a hybridization buffer comprising 0.9M sodium citrate buffer at a temperature of 45°C."

Applicant believes that one of ordinary skill in the art could readily identify useful nucleic acid molecules that hybridize to SEQ ID NO: 1 or SEQ ID NO: 3 under the claimed conditions, particularly in view of the procedures described in the present application.

The instant application describes with particularity the cloning (Example 1), characterization (Examples 2-4), and function (Example 1) of an exemplary plant gene of the present invention that regulates cell division and fruit size in plants. The instant application teaches that the ORFX protein is a soluble protein with an α/β secondary structure (Example 4 and Figure 5A), and a conserved fingerprint shared with the RAX family of proteins, which are known to have wide regulatory functions, including control of cell division (pg. 26, line 27 to pg. 27, line 5). A three-dimensional structure of the predicted ORFX protein was predicted and is disclosed in the instant application (Figure 5A). Homology with twenty-six plant proteins is taught (Example 4 and Figures 4A-B), strongly suggesting that this gene is found in other plants. As a result, applicant's identification and characterization of the proteins that regulate fruit size and/or cell division in plants, as well as the cloning of the encoding genes, would clearly lead others to identify and characterize such proteins and to clone their encoding genes from other plants.

Furthermore, procedures for identification and sequencing of other genes that increase or decrease cell division/plant size in plants would have been readily apparent to those of ordinary skill in the art from applicant's work. For example, DNA fragments that encode the nucleic acid molecule of the present invention could have been used as hybridization probes to remove from libraries of genomic DNA of other plants those fragments likely to encode proteins with similar sequences, e.g., other genes having a RAX family fingerprint, or those which encode proteins showing the patterns of homology to the proteins of the present invention taught in the instant application. Alternatively, knowing the nucleic acid and amino acid sequences of the nucleic acid molecules of the present invention, DNA oligonucleotide primers could be designed and used to remove from libraries of genomic DNA for other plants those fragments likely to encode proteins with similar sequences which increase and/or decrease fruit size and cell division in plants. Thus, based upon applicant's work, it would have been readily apparent to those of ordinary skill in the art how to identify, characterize, and sequence other nucleic acid molecules that regulate fruit size and cell division in plants. With this knowledge, one of ordinary skill in the art could readily make and use the present invention.

Since the claimed invention is fully enabled by the present application, the non-enablement rejection of claims 1-2, 4, 7-8, and 11-49 under 35 U.S.C. § 112 (1st para.) should be withdrawn.

The rejection of claims 1-2 under 35 U.S.C. §102(b) as anticipated by Bowman et al., "CRABS CLAW, A Gene that Regulates Carpel and Nectary Development in *Arabidopsis*, Encodes a Novel Protein with Zinc Finger and Helix-Loop-Helix Domains," Development 126:2387-2396 (1999) ("Bowman") is respectfully traversed in view of the above amendments, incorporating the features of claims 5-7, which have not been rejected based on Bowman, into claim 1.

The rejection of claims 1-2, 4, 8, 12-16, 18, 20, 22-23, 25, 27, 29, 30, 32, 34, 43-44, 46, and 48 under 35 U.S.C. § 102(b) as anticipated by WO 98/42851 to Murray et al. ("Murray") is respectfully traversed in view of the above amendments, incorporating the features of claims 5-7 and claims 9-11, which have not been rejected over Murray, into claims 1 and 8, respectively.

The rejection of claims 1-2, 8, 12-15, 17, 20, 22, 24, 27, 29, 31, 34, 36, 38, and 41 under 35 U.S.C. § 102(b) as anticipated by WO 99/00503 to Yanofsky et al. ("Yanofsky") is respectfully traversed in view of the above amendments, incorporating the features of claims 5-7 and claims 9-11, which have not been rejected over Yanofsky, into claims 1 and 8, respectively.

The rejection of claims 1-2, 4, 12-16, 18, 22-23, 25, 29-30, 32, 36-37, and 39 under 35 U.S.C. § 102(b) as anticipated by Dai et al., "Overexpression of Arabidopsis Hexokinase in Tomato Plants Inhibits Growth, Reduces Photosynthesis, and Induces Rapid Senescence," The Plant Cell 11:1253-1266 (1999) ("Dai") is respectfully traversed in view of the above amendments, incorporating the features of claims 5-7, which have not been rejected over Dai, into claim 1.

The rejection of claims 1, 36, and 43 under 35 U.S.C. § 112 (1st para.) for indefiniteness is respectfully traversed in view of the above amendments.

Finally, at the time of filing said application, applicant submitted an Information Disclosure Statement, together with two PTO-1449 form pages (copy enclosed). Applicant respectfully requests that the cited references be considered, that the PTO-1449 pages be initialed to indicate that the cited references were considered, and that the initialed PTO-1449 pages be sent to applicant's undersigned attorney.

In view of all of the foregoing, applicant submits that this case is in condition for allowance and such allowance is earnestly solicited.

Respectfully submitted,

Date: February 5, 2003

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February 5, 2003 (Date) JoAnn Whalen

Appendix A

Version With Markings to Show Changes Made

In reference to the amendments made herein to claims 1, 5-8, 36, and 43 additions appear as underlined text, while deletions appear as bracketed text, as indicated below:

1. (Amended) An isolated nucleic acid molecule encoding a protein which [regulates] reduces fruit size and/or cell division in plants, wherein the nucleic acid molecule either: 1) has a nucleotide sequence of SEQ. ID. No. 1; 2) encodes a protein having an amino acid sequence of SEQ. ID. No. 2; or 3) hybridizes to a nucleic acid molecule having a nucleotide sequence of SEQ. ID. No. 1 under stringent conditions characterized by a hybridization buffer comprising 0.9M sodium citrate buffer at a temperature of 45°C.

5. (Amended) An isolated nucleic acid molecule according to claim 1 [4], wherein the nucleic acid molecule has a nucleotide sequence of SEQ. ID. No. 1.

6. (Amended) An isolated nucleic acid molecule according to claim 1 [4], wherein the nucleic acid molecule encodes a protein having an amino acid sequence of SEQ. ID. No. 2.

7. (Amended) An isolated nucleic acid molecule according to claim 1 [4], wherein the nucleic acid molecule hybridizes to a nucleic acid molecule having a nucleotide sequence of SEQ. ID. No. 1 under stringent conditions characterized by a hybridization buffer comprising 0.9M sodium citrate buffer at a temperature of 45°C.

8. (Amended) An isolated nucleic acid molecule [according to claim 1], wherein the nucleic acid molecule encodes a protein which increases fruit size and/or cell division in plants, and the nucleic acid molecule either: 1) has a nucleotide sequence of SEQ. ID. No. 3; 2) encodes a protein having an amino acid sequence of SEQ. ID. No. 4; or 3) hybridizes to a nucleic acid molecule having a nucleotide sequence of SEQ. ID. No. 3 under stringent conditions characterized by a hybridization buffer comprising 0.9M sodium citrate buffer at a temperature of 45°C.

Appendix A

Version With Markings to Show Changes Made

36. (Amended) A method of decreasing [regulating] fruit size in plants comprising:

transforming a plant with a nucleic acid molecule according to claim 1 under conditions effective to decrease [regulate] fruit size in the plant.

43. (Amended) A method of decreasing [regulating] cell division in plants comprising:

transforming a plant with a nucleic acid molecule according to claim 1 under conditions effective to decrease [regulate] cell division in the plant.